

Thesis for doctoral degree (Ph.D.)
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Better Balance with Somatosensory Exercises — a Parkinson Perspective



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Better Balance with Somatosensory Exercises — a Parkinson Perspective

By

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This thesis was written for all those who have once lost their foothold in life
(as when getting diagnosed with a severe disease),
and whose only hope is
to keep on fighting.

ABSTRACT

BACKGROUND People with Parkinson's Disease (PD) experience increasing activity limitations in walking, carrying objects, turning around, and dressing. Subtle and often unconscious balance decline may have occurred already at an early stage, even when first diagnosed. At present, no medical treatment can ease the progressive balance impairment. Instead, physical training has become a means to remain physically active and mobile for as long as possible.

AIM The overall aim of this thesis was to evaluate if our hypotheses, the training approach of 'Somatosensory Focused Balance Training without Cues', can be effective in supporting people with PD at an early stage (early PD) to maintain their balance ability, so that they can remain physically active, move and walk independently, for as long as possible.

METHODS At first, the BDL Balance Scale, a clinical balance assessment, was validated for use in people with early PD. Thereafter, to investigate the effect of 'Somatosensory Focused Balance Training without Cues', people with early PD (n=28) were randomised into two training groups and tested by a blinded assessor before and after the intervention. The training was evaluated with clinical outcomes, laboratory movement outcomes and the result was compared to healthy age-matched controls (n=18). Furthermore, to acquire knowledge of how people with early PD perceived the intervention, an interview study using content analysis was performed.

RESULTS The BDL Balance Scale was found to be valid for use in early PD. It correlated to similar scales and could detect a difference between early PD and healthy controls. The training approach improved balance in the studies population, measured with clinical and movement laboratory outcomes, as well as by participant perceptions. The interviews provided important information on how the group contributed to greater motivation for training and offered a platform for making new friends.

CONCLUSION The 'Somatosensory Focused Balance Training without Cues' improves balance in early PD. Notably, the training context is particularly important considering that it can increase the motivation and compliance to the training. In order to understand the underlying mechanisms for the improved balance, further research is needed.

SAMMANFATTNING

BAKGRUND Parkinsons sjukdom leder till successivt tilltagande motoriska svårigheter som till exempel att gå, kunna bära saker, kunna vända runt och att klä på sig. Redan när diagnosen ges, och i ett tidigt skede förekommer en subtil, ofta omedveten balansnedsättning. För närvarande finns det ingen medicinsk behandling som kan motverka påverkan på balansen. Istället har träning blivit ett medel att försöka bibehålla sin aktivitetsförmåga.

SYFTE Det övergripande syftet med detta projekt var att utvärdera om vår träningshypotes "Somatosensory Focused Balance Training without Cues" är en effektiv metod för att stötta personer med Parkinsons sjukdom i tidigt skede (tidig Parkinson) att bibehålla sin balansförmåga, så att de kan förbli fysiskt aktiva samt gå och röra sig självständigt så länge som möjligt.

METOD För att kunna utvärdera balansförmågan vid tidig Parkinson validerade vi BDL Balansskala, ett kliniskt test. Därefter, för att utvärdera effekten av "Somatosensory Focused Balance Training without Cues", lottades personer med tidig Parkinson (n = 28) till två träningsgrupper. Träningen utvärderades med kliniska test och laboratoriebaserad rörelseanalys, dessutom jämfördes resultaten mot friska åldersmatchade deltagare (n = 18). För att få kunskap om hur deltagarna själva upplevde träningen gjordes också en intervjustudie med innehållsanalys som metod.

RESULTAT För personer med tidig Parkinson visade sig BDL Balansskala vara ett valitt test att använda. Skalan korrelerade med liknande balansskalor och kunde detektera en skillnad mellan deltagarna med tidig Parkinson och de friska deltagarna. Vår träningsmetod "Somatosensory Focused Balance Training without Cues" förbättrade balansen hos deltagarna med tidig Parkinson utvärderat med kliniska test och rörelseanalys. Detta bekräftades också av deltagarnas egna berättelser i intervjustudien. De gav dessutom viktig information om träningens upplägg, som att gruppträning gav ökad motivation till att träna och dessutom bidrog till nya vänskapsrelationer.

SLUTSATS "Somatosensory Focused Balance Training without Cues" förbättrar balansen hos personer med Parkinsons sjukdom i tidigt skede. Träningskontexten är särskilt viktig att beakta eftersom den kan bidra till ökad motivation och bättre följsamhet till träning. För att förstå de underliggande mekanismerna till att balansen förbättrades av träningen behöver ytterligare forskning göras.

LIST OF SCIENTIFIC PAPERS

- I. Claesson IM, Grooten WJA, Lökk J, Ståhle A. *Assessing postural balance in early Parkinson's Disease – validity of the BDL balance scale*. *Physiother Theory Pract* 2017; 33: 490–6.
- II. Claesson IM, Ståhle A, Lökk J, Grooten WJA. *Somatosensory Focused Balance Training without cues can improve balance and gait in early Parkinson's disease – a randomised pilot study*. *European Journal of Physiotherapy* 2017; DOI: 10.1080/21679169.2017.1363284
- III. Claesson IM, Sobel J, Grooten WJA. *Improved Dynamic Balance in early Parkinson's Disease – Movement Analysis using the Alternate Step Test*. Submitted for publication.
- IV. Claesson IM, Ståhle A, Johansson S. *The Group is the Glue – perceptions of group exercise among people with early Parkinson's disease*. Submitted for publication.

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LIST OF ABBREVIATIONS

BBS	Berg Balance Scale
BDL	Bäckstrand Dahlberg Liljenäs Balance Scale
CoM	Centre of Mass
CoP	Centre of Pressure
Early PD	Parkinson's Disease at an early stage (H&Y<3)
fMRI	Functional Magnetic Resonance Imaging
H&Y	The Hoehn & Yahr Parkinson's Disease staging scale
ICF	The International Classification of Functioning, Disability and Health
MMSE	Mini Mental State Exam
MRI	Magnetic Resonance Imaging
mUPDRS	the motor part of the Unified Parkinson's Disease Rating Scale
n.s.	Non significant
PD	Parkinson's Disease
TuG	the Timed Up and Go test
TuG-cog	the Timed Up and Go-cognition test
UPDRS	The Unified Parkinson's Disease Rating Scale



PROLOGUE*

"I have lived with Parkinson for many years now", she said.

*"So many times that I have wished for a cure ...
I still dream about walking like a normal person again".*

She continued:

*"Now I have accepted Parkinson as my companion,
telling me when and how to do things.*

I can no longer decide all by myself, I have to remember to ask 'Mr Parkinson';

*"- Will you please let me walk straight and lift my legs properly,
so that I won't draw attention to myself?"*

"- And please see to that my hands won't start to shake at the restaurant!!!"

**These are personal memories from meetings in the clinic over the years
(...more to come)*

1 INTRODUCTION

The focus of this thesis was the search to find an effective balance training method to improve the balance ability of people with Parkinson's Disease (PD) by exercise.

1.1 CONCEPTUAL FRAMEWORK

The International Classification of Functioning, Disability and Health (ICF) ^{1, 2} is used in the thesis (Figure 1) in order to provide a standardised terminology and classification of the consequences of PD. The ICF conceptualises functioning and disability in the context of health as a “dynamic interaction between a person's health condition, environmental factors and personal factors”.

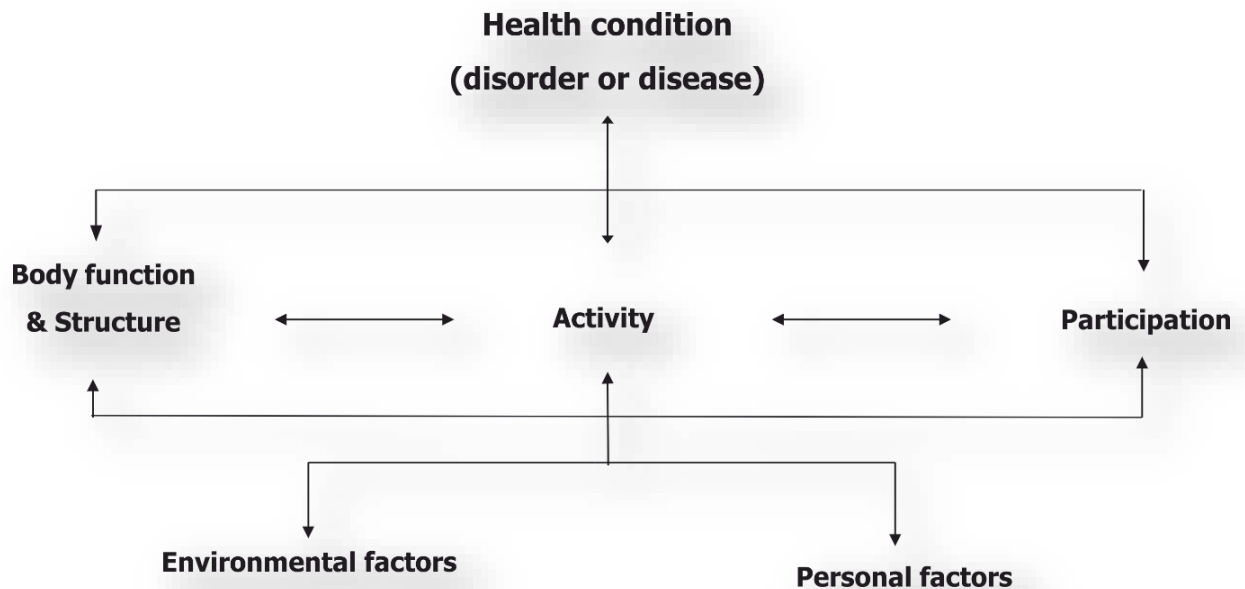


Figure 1. The model of the International Classification of Functioning, Disability and Health (ICF).

1.2 PARKINSON'S DISEASE

People with PD are found worldwide and it is the second most common neurodegenerative disorder, affecting approximately 1.5 percent of the population in Europe, with an increasing prevalence with older age ³. Much remains to be understood about its causes and underlying pathology. Many researchers believe that PD emerge due to an interaction between genetic and environmental factors that leads to the progressive degeneration of neurons of the brain ³. Primarily, PD is regarded as a hypo-dopaminergic disease, with symptoms mostly due to loss of dopamine producing neurons in the substantia nigra, a part of the basal ganglia ⁴.

The disease is characterised by various motor and non-motor symptoms with a progressive impairment in different components of function. The motor manifestations comprise the cardinal symptoms; bradykinesia, rigidity, tremor, and postural instability (impaired balance).

Non-motor manifestations include autonomic disturbances, sleep disturbances, cognitive decline and a range of neuropsychiatric expressions. The diagnosis of PD is made from the clinical manifestation of bradykinesia together with one of the other cardinal symptoms, usually tremor or rigidity ⁵.

For people diagnosed with PD, medical treatments can only partially ease their symptoms. Even with an optimal health care management, people with PD experience a progressive decline in their autonomy and an increasing disability in gait, balance, and posture. At present, therapeutics available for people with PD, offer only symptomatic relief, and there are no known medications to prevent its onset, or to slow down or freeze the disease progression ⁶. At early stage, medication is a powerful tool for easing the symptoms. However, motor fluctuations related to time since medicine intake are common, especially after long term medication ⁷.

Raggi et al. ⁸ have described function in people with PD at an outpatient clinic using the ICF. The most frequent self-reported limitations on activity and participation were in the activity areas, namely walking (94%), lifting and carrying objects (92%), and dressing (91%). They found that the limitations were mainly caused by the impairments in body function and not to any greater extent influenced by environmental or personal factors.

Recent studies have shown that people with PD who self-reported regular exercise of more than 2.5 hours/week after the disease onset had a slower decline in function compared to those who exercised less ⁹.

1.3 MEASURING DISEASE SEVERITY

Disease severity is usually classified in the clinics by the Hoehn & Yahr Scale (H&Y) ¹⁰ and the Unified Parkinson's Disease Rating Scale (UPDRS) ¹¹.

1.3.1 Hoehn & Yahr Staging Scale

The H&Y scale offers a quick and easy screening test for Parkinson's disease severity, based on motor function only. The scale ranges from no signs of disease, stage 0, to wheelchair bound or bedridden, stage 5 (Figure 2). Stages 1-2 correspond to one-sided, and mild bilateral symptoms without balance impairment, respectively. Stage 3 is used when people are still physically independent, but balance impairment is identified (judged by the recovery on the pull test ¹²). Stage 4 classifies persons with severe symptoms, but who are still able to walk or stand unassisted. In this thesis we used the modified H&Y scale that includes 0.5 increments ¹³. The thesis pertains to people with idiopathic PD at an early stage (early PD), defined as H&Y < 3 ^{5, 14}.

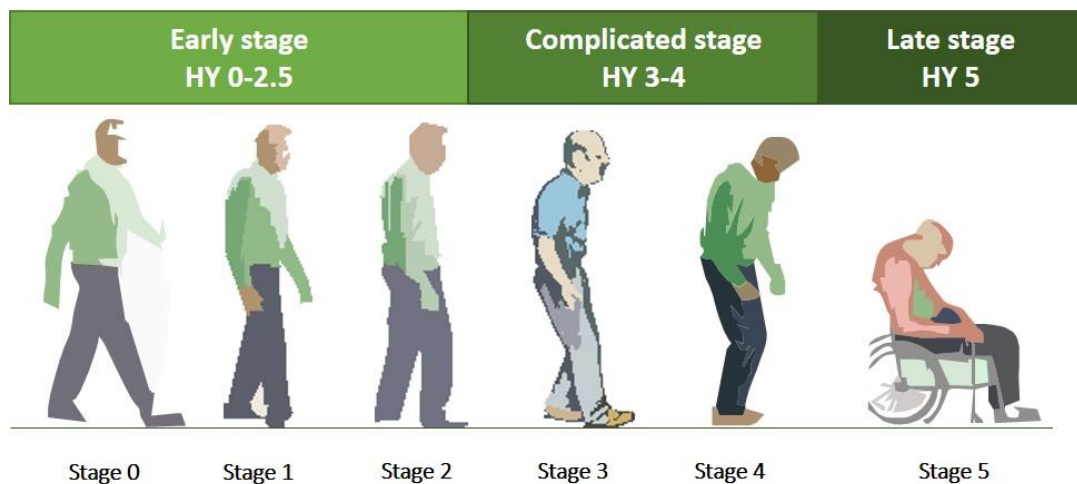


Figure 2. The Hoehn & Yahr scale classifying different stages of Parkinson's Disease. The blue shirted man in stage 3, shows the dividing point of when the pull test becomes positive. Illustrated by I Claesson.

1.3.2 Unified Parkinson's Disease Rating Scale

Compared to H&Y, the UPDRS is a more detailed examination of the disease severity. This has become the gold standard for clinical evaluation of impairment in PD. Assessments include the following areas:

- I. Mentation, behaviour and mood
- II. Activities of daily living
- III. Motor examination (mUPDRS)
- IV. Complications of therapy

The mUPDRS was used in our studies in addition to the H&Y. Here, the assessor screens for motor symptoms (tremor, coordination, posture etc.) with a maximum severity of 108 points. Postural instability can influence the result by a maximum of eight points (if the gait item is included). The postural stability item is judged based on recovery on the pull test, as in H&Y.



“What about your balance?”, I asked.

“There is nothing wrong with my balance!”, she answered indignantly.

“I remember you telling me that you fell....?”, I continued.

“Well, that had nothing to do with Parkinson!

It was just because it was slippery outside!”

I replied;

*“Didn’t you tell me that you had stopped biking and jogging, why is that?
And that you need to sit down when putting on your socks and trousers?”.*

“Hmmm....” She gave me a pensive look.

1.4 BALANCE

The term balance control can be described as keeping control over the body while changing body position (as in walking or in body transfers) or while maintaining body position (as in sitting and standing). It is imperative to have control of your body Centre of Mass (CoM) in order to perform activities in daily life ¹⁵. When growing old, balance ability declines, even if healthy ¹⁵.

Balance and postural stability are obtained from a complex neuro-motor integrative system where both sensory, motor and cognitive functions are involved, and they relate to our body's orientation in space and the environment ¹⁶, as described in Figure 3. The input and feedback via our sensory system (somatosensory, vestibular and visual) adjusts the final motor adjustment.

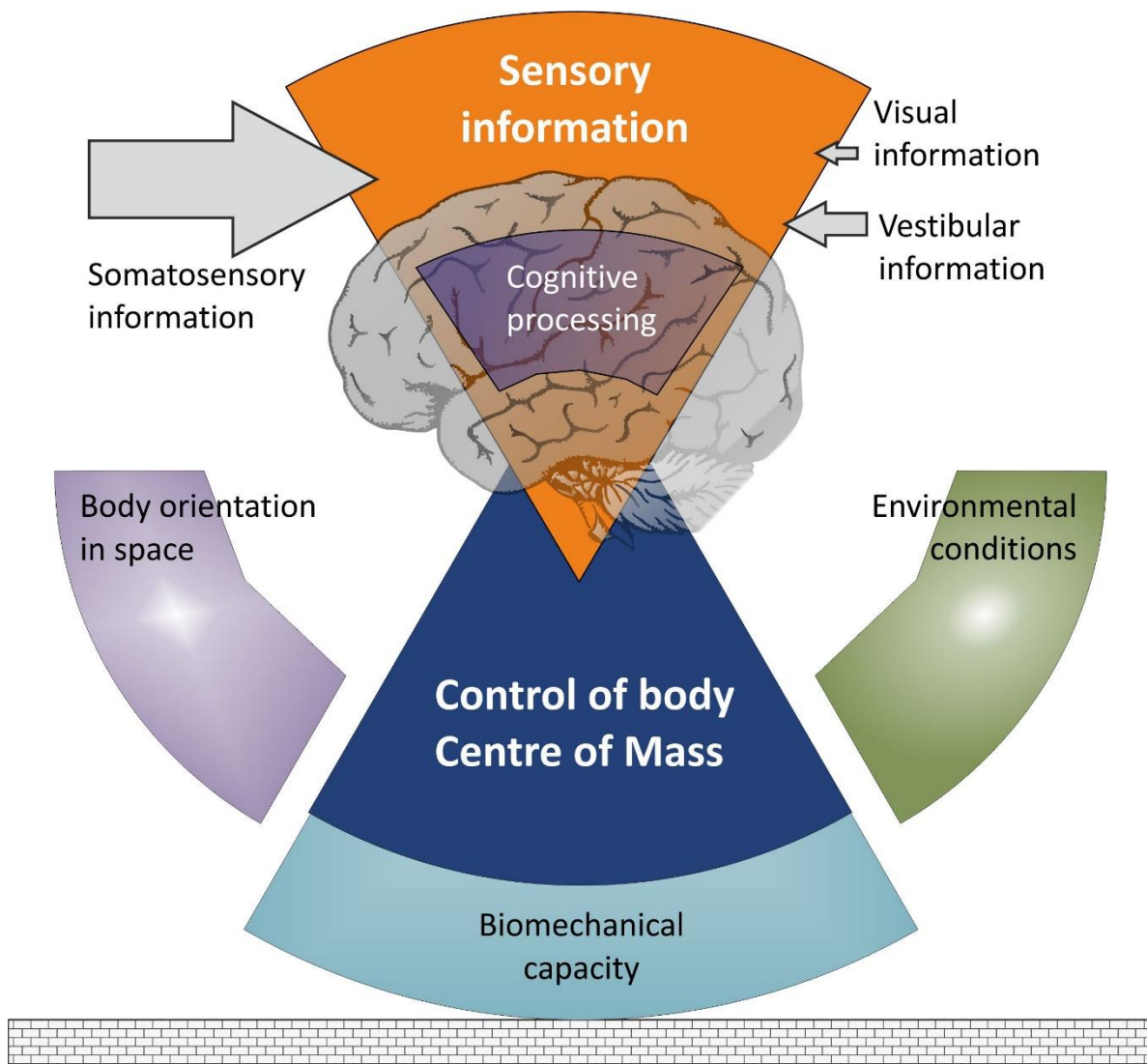


Figure 3. Balance organisation model. The interplay between components involved for balance control in healthy people standing on a firm surface. Illustrated by I Claesson.

1.4.1 Balance in Parkinson's Disease

All or some of the balance components described in Figure 3 may be dysfunctional in people with PD, rendering balance impairment a severely disabling factor ¹⁷. For example, muscular rigidity reduces the biomechanical capacity, bradykinesia affects how to adjust oneself according to the environment, and the cognitive processing (primarily in the later stages of PD) impairs dual task performance, like, for example, walking while talking. Even when PD is first diagnosed, subtle balance problems can be measured, such as increased postural sway and slowed turning ¹⁸. Over time, the severity of balance problems increase. The present thesis concentrates on the sensory information system, which has been proven to be impaired already in early PD ¹⁹.

1.4.2 Sensory System in Balance Control

The sensory system receives all the information needed for balance control from the body and the environment (Figure 3). It is used to initiate, supervise and monitor ongoing movements. There are three subsystems; i) the somatosensory (tactile and proprioceptive), ii) the vestibular, and iii) the visual.

Feedback from the three sensory subsystems are integrated so as to generate a corrective movement response by activating our muscles. On a firm surface, healthy people normally rely approximately to 70 percent on somatosensory information, to 20 percent on vestibular information and to 10 percent on visual information (Figure 3) ²⁰. Specifically, a dysfunctional integration of proprioception has been proposed to play a major role in the pathophysiology of balance disorders in PD ^{21, 22}.

1.4.2.1 *The somatosensory subsystem for balance*

The somatosensory subsystem (tactile and proprioception) is used for body adjustments when moving. Abnormalities in proprioception manifests as deficits in kinaesthesia, which is the conscious awareness of limb and body position, motion and orientation in space.

Of all the subsystems of sensory information, the proprioceptive information has the shortest time delay before onset. The monosynaptic pathways can process information as quickly as 40–50 ms, and, therefore, proprioception forms the major contributor of sensory information for balance in healthy people ²³.

If somatosensory information is unavailable or ambiguous, a process of reweighting reliance towards the visual or vestibular subsystems occur ²⁴. As mentioned earlier, when standing on a solid surface with eyes open, somatosensory input is said to supply approximately 70 percent of the balance sensory information, but when standing on an unstable surface with eyes closed, vestibular input becomes the main provider of information ²³. In PD, the impaired integration of the somatosensory information for balance control is said to result in a reweighting and overreliance on the visual input ^{25, 26}.

1.4.2.2 Somatosensory subsystem in Parkinson's Disease

Already in 1998, Rossini et al.²⁷ investigated the proprioception in PD by looking at the responsiveness to sensory stimuli, and tested with electrical somatosensory evoked potentials from the frontal scalp. They showed that people with PD, even at the early stages of the disease, had severely depressed responsiveness to these somatosensory stimuli.

This was further investigated by Adamovitch et al.²⁸ who established that subjects with PD had particularly difficult in performing an unfamiliar task that required integration between sensory subsystems in order to acquire the target. In particular, they had difficulties in accurately pointing with an unseen limb to a steadily illuminated target in the dark, a task that could easily be performed with the use of the visual and proprioceptive input in combination.

Furthermore, Keijsers et al.²⁹ repeated a similar study in which people had to point to a remembered visual target with and without visual feedback. Their study indicated the existence of a proprioceptive information-processing deficit in PD, and concluded that it had developed even at an early stage of the disease.

Moreover, people with PD have difficulty in perceiving small changes in surface inclination¹⁹. For example, Vaugoyeau et al.³⁰ found that PD subjects standing on a slowly tilting platform with their eyes shut could better control their body CoM if they at the same time had a vibration stimulus, reinforcing proprioceptive information, on the ankle muscles. They also hypothesised that the flexed posture in PD (stooped posture, pisa-syndrome or camptocormia), is at least partly associated with the sensorimotor integration impairment in PD. This is in line with the findings of Zia et al.³¹ who also concluded that the proprioceptive impairment might contribute to the problems with posture encountered in PD. For this reason, additional analysis of the effect from “Somatosensory Focused Balance Training without Cues” on posture, will be presented exclusively in this thesis (the heading 4.2.1.1).

In summary, the somatosensory deficit leads to difficulties integrating the somatosensory feedback with visual feedback, as earlier described, in, for example, reaching for a visible object without eye vision of the arm or standing on a tilting board. Such impairments increase the dependence on visual cues during movements³². Consequently, this deficit seems to result in an overreliance of the visual input when moving in people with PD²⁶.

1.4.3 The Control of Body Centre of Mass

Maintaining balance involves keeping control of your body CoM, based on the information from the sensory system. The better your balance control, the better you can act and adjust to changes in the base of support while moving, standing, transferring, or balancing on a steady or moving base of support. The balancing challenge differs according to whether you are in a stationary or a moving situation.

1.4.3.1 Static and Dynamic Balance

Static balance is the ability to maintain the CoM over the base of support when being still, as in standing or sitting down. Even when standing still there is a postural sway, an ongoing work in keeping the body CoM within your base of support.

Dynamic balance is the ability to control the transition of body CoM while you are in motion, as in getting up from a chair, walking, dancing, etc. According to Ashburn et al.³³ the most common activity conducted when falling in people with PD is walking.

1.4.3.2 Stability Limits and Centre of Pressure

Maintaining an upright stance requires control of the momentum and the position of the CoM over the base of support. Balancing strategies can either be anticipatory (planned adjustment like stepping gently over an icy spot) or reactive (reaction to perturbation), and may lead either to a fixed-support or to a change-in-support response. The ‘Stability Limits’ denote the maximum range in which the CoM can be moved without a change in the base of support. People with PD have reduced stability limits compared to healthy people³⁴.

When standing, all forces acting between the feet and the ground can be summoned to yield a single ground reaction force vector and a torque. The point of application of the ground reaction force is the Centre of Pressure (CoP). A person’s stance stability/flexibility may be quantitatively assessed through measurements of the trajectory of the CoP³⁵, used in this thesis Study III.

1.4.4 Measuring balance in PD

Clinical tests of balance can assess different components of the balance. Health professionals should be aware of what component is measured. To our knowledge, there is no gold standard for measuring balance in PD.

The recommended clinical measures of postural stability and balance in PD are often developed for use in the more severe balance problems that appear at the later stages of the disease. It is not clear whether these tests can be used to detect postural instability at the early stages. Many of the recommended gait and balance tests for PD reach a ceiling effect when used in early PD¹⁴.

The outcome measures for evaluating balance performance in PD, recommended in the ‘European Physiotherapy Guideline for Parkinson’s Disease’¹⁴ are; ‘Modified Parkinson Activity Scale’, ‘Timed Up & Go’ (TuG), ‘Mini-BESTest’, ‘Dynamic Gait Index’, ‘Functional Gait Assessment’ (FGA), ‘Berg Balance Scale’ (BBS), ‘Five Times Sit to Stand Test’ (FTST) and the ‘Push and Release Test’. The tests can be disputed as being tests solely of balance, since they are also influenced by other factors such as strength (FTST) and gait (FGA, TuG) or limited to one interacting part of the balance components like the ‘Push and Release Test’, a test of the reaction to a perturbation. Also, many of the tests have a well-

documented ceiling effect when used for people with minor to moderate balance disorders^{14, 36, 37}, as shown for the BBS in Figure 4.

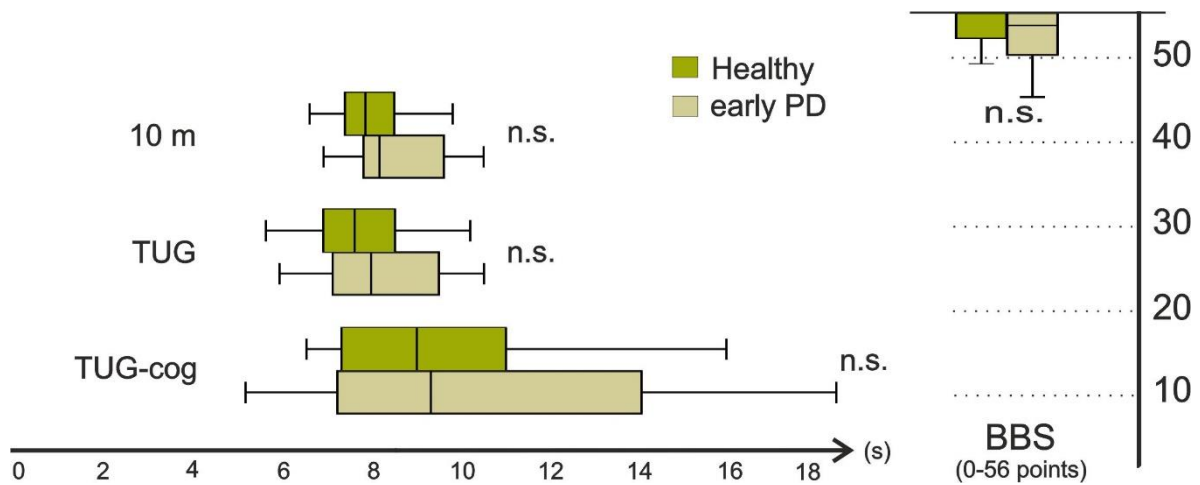


Figure 4. Boxplots (medians and interquartile range) showing result from early PD ($n=14$) and matched controls ($n=14$) performing the 10 m walk test (10 m), the Timed Up and Go test (TuG), the Timed Up and Go-cognition (TuG-cog), and the Berg Balance Scale (BBS). Data analysis from participants included in the thesis.

n.s. = non-significant, $p>0.05$.

At the start of the work with this thesis, we compared the result from some of the most frequently used clinical outcome measures, between people with early PD and age- and sex-matched controls (Figure 4 and Table 1). The measures used could not reveal any significant difference between early PD and controls, indicating that these outcome measures are not sensitive enough to detect balance problems for this population. Consequently, a more challenging test was needed for use in balance evaluation of people with early PD³⁷⁻³⁹. This led to the validation of the BDL balance scale in the Study I.

Table 1. Non-parametric statistics between early PD and age- and sex-matched controls performing clinical balance assessment tests. The table is based on the participants included in the thesis.

TEST	Controls (n=14)/ early PD (n=14)*
Berg Balance Scale	$p=0.21$
Eight of Balance	$p=0.08$
10 m walk	$p=0.11$
Timed Up and Go	$p=0.43$
Timed Up and Go-cog	$p=0.80$

*Mann Whitney U test,
 $p<0.05$

1.4.5 Neuroplasticity

Neuroplasticity is defined as the ability of the brain to undergo structural and functional change in response to new experiences as for example exercise ⁴⁰. It has been demonstrated in humans with different techniques, for example measuring the regulation of the brain-derived neurotrophic factor (BDNF) or with functional Magnetic Resonance Imaging (fMRI) (measuring changes in activation and recruitment of brain areas involved in movement) ⁴¹.

The brain's ability to adapt has allowed humans to specialise in specific motor skills based on relative use and activity. For example, a right-handed person may perform a movement poorly with their left hand, but continuous practice with the non-dominant hand can make it just as able. Another example is people without hands who are capable of retrieving much of their lost function by practicing and “rewiring” the brain in order to incorporate lost hand abilities by using their feet ⁴²⁻⁴⁴.

That structural neuroplasticity can arise also in elderly people, was shown by Draganski et al. ⁴⁵. They divided a homogeneous group, more than 60 years of age, into two gender-matched groups: training and control. Both groups were inexperienced in terms of juggling. The training group was given three months to learn classic three-ball cascade juggling. In the results they found training-induced grey matter increase within the brain. Similarly, Boyke et al. ⁴⁶ found that plasticity of the human brain is preserved even in later years, and their data support conclusions about exercise for elderly people with the purpose to ‘train the brain’ in order to avoid ‘draining of brain’.

Gauthier et al. ⁴⁷ evaluated whether evidence could be found for structural brain changes due to training. People with chronic stroke symptoms were assigned to constraint-induced movement therapy and structural Magnetic Resonance Imaging (MRI) scans were performed immediately before and after therapy. The group exhibited great improvement in using the more affected arm in daily life activities in parallel with structural brain changes. Their findings suggest that in chronic stroke, structural remodelling of the human brain was facilitated by constraint-induced movement therapy, a condition once thought to be refractory to treatment ⁴⁷.

Will structural brain alterations be promoted in PD by motor training and motor learning? Although, this mystery remains unanswered, the findings described in healthy elderly people and in people with chronic stroke symptoms provide compelling evidence that all human brains undergo morphological alterations in response to learning and/or rehabilitation, and evidence is growing in studies of people with PD as well ^{48,49}.

1.5 PHYSIOTHERAPY IN PARKINSON'S DISEASE

Physiotherapy interventions are considerably varied when it comes to PD. Interventions focus on mobility, transfers, posture, upper limb function, balance, gait, and physical capacity. The therapist uses exercises added with cueing strategies and cognitive movement strategies in order to maintain or increase independence, safety, and quality of life. The sensory cueing strategies, e.g. auditory, tactile, and visual, are often used to help movement initiation and walking^{14, 50}.

The 'European Physiotherapy Guideline for Parkinson's disease'¹⁴ recommends and have found strong evidence for:

- Conventional physiotherapy to improve walking speed, muscle strength and movement functions
- Treadmill training to improve walking speed and stride length
- Tai-chi to improve movement functions
- Cueing for gait (auditory or visual) to improve gait speed
- Movement strategies for complex motor sequences to improve functional mobility

According to the guidelines, there is yet no intervention showing strong evidence of improved balance in PD although evidence of a weak positive effect on balance was established for the interventions mentioned¹⁴. Consequently, there is no recommended optimal approach for improving balance in PD. To establish the best practice for improving balance in PD is not yet possible. However, earlier research definitely favours exercise compared to no exercise⁵¹⁻⁵³. Recent studies of highly challenging balance exercise, dancing exercise and tai chi show promising results⁵⁴⁻⁶⁰.

A future challenge is to design and support appropriate interventions within the social and health care sector to maintain activity and participation skills for this population during disease progression for as long as possible.

1.6 PARADIGM

Recent research indicates the presence of neuroplasticity changes in chronic neurological disorders. An emerging body of evidence suggests that exercise can trigger several neuroplasticity changes in the human PD brain^{49, 61}. This thesis is based on the hypothesis that such changes are possible for people with idiopathic early Parkinson's disease.

1.7 RATIONALE

Research suggests that the movement disorder in PD is associated with a deficient integration of somatosensory information used to construct the internal representation of the body position and motion in space, leading to an impaired balance control. Since information from the balance somatosensory subsystem in PD is said to be affected even at an early stage of the disease, and reweighted towards the visual subsystem, the following questions arose:

In light of the growing evidence for neuroplasticity changes by exercise in PD ^{49, 61}, can the integration of balance somatosensory subsystem be reinforced and improved by targeted exercises?

The cueing strategies used for people with PD, most often visual or auditory, do they not reinforce the constraint use of somatosensory input, and are they, therefore, counterproductive?

1.8 RESEARCH QUESTION



Does our hypothesis-based training approach, the ‘Somatosensory Focused Balance training without Cues’ (that imposes the use of somatosensory integration for balance control), improve balance and movement in people with early Parkinson?

2 AIMS

2.1 LONG TERM GOAL AND OVERALL AIM

The long term goal of this thesis was to find an effective balance training method for people with early PD, so that they can remain physically active and independent for as long as possible. We therefore strived to expand the knowledge of how to improve their balance, and particularly in association with voluntary movement and gait. Our means to realise this was through exercise.

Our exercise hypothesis, to be evaluated in the thesis, was based on the idea of giving focused input to the presumed affected system in order to induce neuroplasticity. This was inspired by the idea of constraint induced therapy in stroke. Consequently, a physiotherapy intervention, targeting the motor relearning with regard to the integration of somatosensory feedback for the control of balance, was needed.

2.2 SPECIFIC AIMS

To this end, and based on the hypothesis, we developed an exercise protocol, the ‘Somatosensory Focused Balance Training without Cues’, described in the thesis appendix. Furthermore, to enable us to evaluate the result from the training, we needed to find a valid and reliable clinical balance scale that could assess balance performance in early PD. We also investigated whether the balance training did contribute to any changes in laboratory-measured movement outcomes. Finally, we were interested in the participants’ own perception of the intervention.

As a consequence, four studies were needed to be carried out; a validity study, a clinical randomised balance training study, an experimental laboratory movement analysis study, and a qualitative interview study.

The specific aim of each study was:

Study 1. To explore the validity of the BDL balance scale, for use in people with early PD.

Study 2. To evaluate the effect of the balance training intervention, ‘Somatosensory Focused Balance Training without Cues’, in people with early PD using clinical balance outcomes.

Study 3. To evaluate the effect of ‘Somatosensory Focused Balance Training without Cues’ in people with early PD before and after the exercise intervention, and compared to healthy controls, using laboratory movement analysis outcomes.

Study 4. To acquire knowledge of how people with early PD regarded group exercise in general, and their perceived effect of the ‘Somatosensory Focused Balance Training without Cues’.



“What about if we put together a balance exercise programme for you?”, I asked.

“Oh, that’s not needed; my physio said that my balance is perfect.

I scored full on the Berg Balance Scale!”

I continued: “That’s indeed very good, but then we need to find another scale that is more up to your level. Only when we have found a suitable scale, are we able to evaluate your balance performance before and after training!”

“That’s typical, you people in health care, you always want to measure...”, she replied, giving me a funny face.

I continued exalted; “We could even take you in to our movement laboratory and compare your movements to healthy people, and even more, we can investigate whether the exercise influenced your movement performance!”

Now I was almost shouting in euphoria.

She answered; “I know to myself if I’m getting better or not, you just have to ask me!”

She looked at me as if she thought I was an idiot.

“Good idea!”, I replied. “I will do that as well!”

3 SUBJECTS AND METHODS

3.1 DESIGN AND PARTICIPANT FLOW

The feasibility of the intervention was tested prior to the thesis by the research group (n=4, early PD, non-published). Using the laboratory data from this analysis, the required sample size was calculated.

The overall design was a randomised cross-over training study for people with early PD. In parallel we recruited a control group of healthy age- and sex-matched people, see Figure 5. Nevertheless, due to drop-outs, leading to low power in Study II and III, data from the two training groups needed to be merged for analysis.

Study I had a cross-sectional design and was carried out using data from the eligibility assessment of people with PD together with an age- and sex-matched subgroup within the healthy control group.

*Study II** had a randomised controlled cross-over design. It was derived using the clinical data of the pre- and post-assessments together with the follow-up assessment. Computerised randomisation into training groups was made by the training instructor, after the eligibility assessments, and was kept secret until all post-assessments were made. This was to ensure the assessor to be blinded of whether the participant had yet taken part in the training or not.

*Study III** had a randomised controlled cross-over and a cross-sectional design. It was derived using the laboratory movement analysis data of the pre- and post-assessments together with the healthy controls assessment.

*Study IV** had a qualitative design of content analysis. All participants in the delayed start group were included regardless of their attendance to the training.

The supplementary thesis analysis was derived from the same data as in Study III.

*One person that dropped out from the immediate start group, was included again in the delayed start group. For validity reasons, this person was excluded from the clinical and laboratory evaluations (Study II - III). However, the person took part in the Study IV.

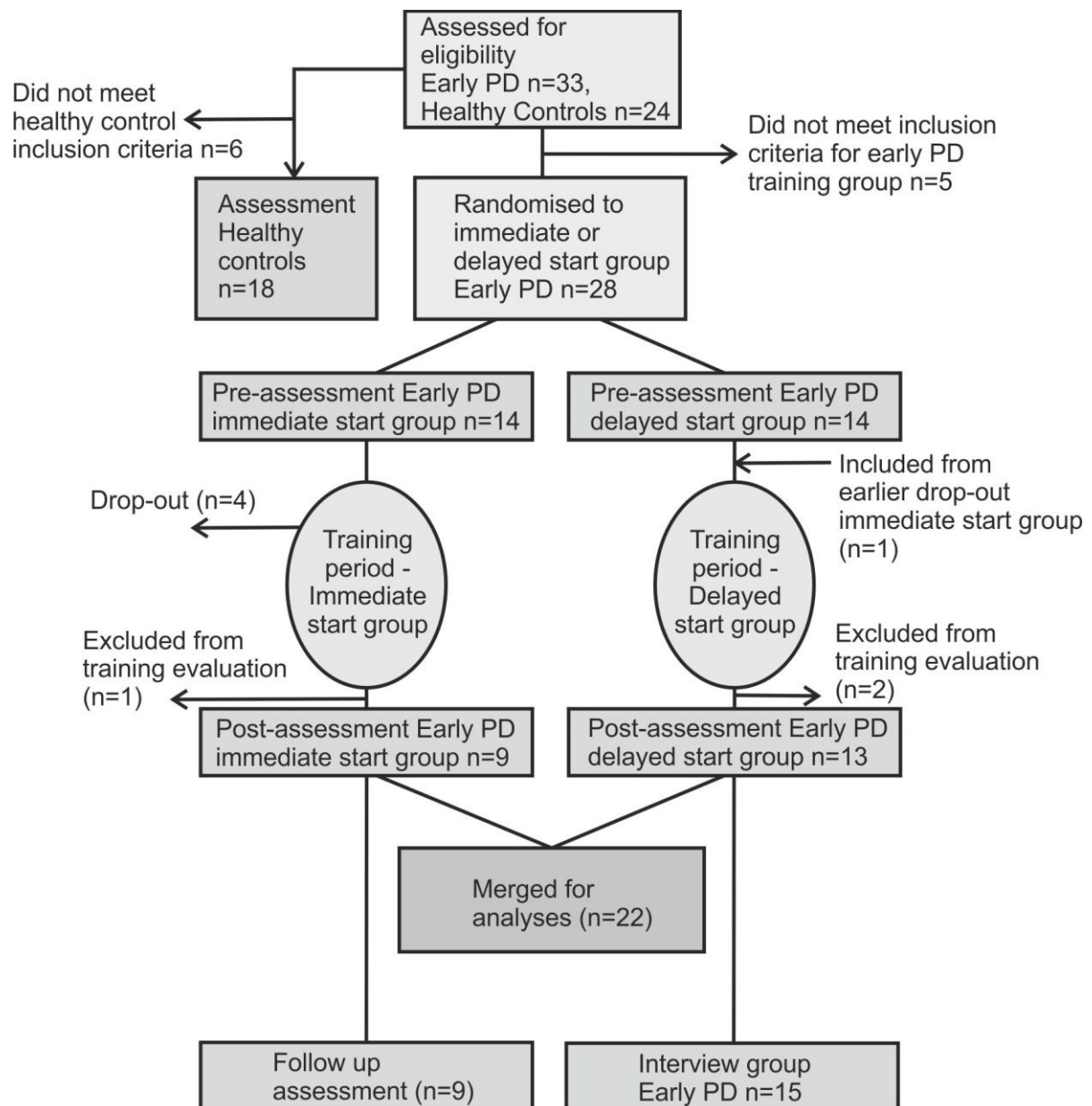


Figure 5. Enrolment, participant and assessment flow.

3.2 PARTICIPANTS

Having read the advertising, either at one out of 16 neurological clinics in Stockholm or at the associations for seniors in Stockholm County, the participants volunteered by contacting us. After an assessment of eligibility, 28 people with early PD, established by their neurologist, (median (md) H&Y stage 2, md age 69 years, 17 females/11 males), and 18 healthy controls (md age 75, 11 female/7 male) were included.

Inclusion criteria for the early PD participants were community-dwelling, ambulating people with no walking aids, having a stable parkinsonian medication, and no other history of orthopaedic or neurological disorder other than PD that could affect motor performance. Moreover, they should not have any sensory deficit in the lower extremities when bedside screened. The healthy participants were equally included, apart from the PD diagnosis and the medication criteria.

For the training intervention, only the participants with early PD were included. The characteristics of a fictive, representative person is presented in Figure 6.

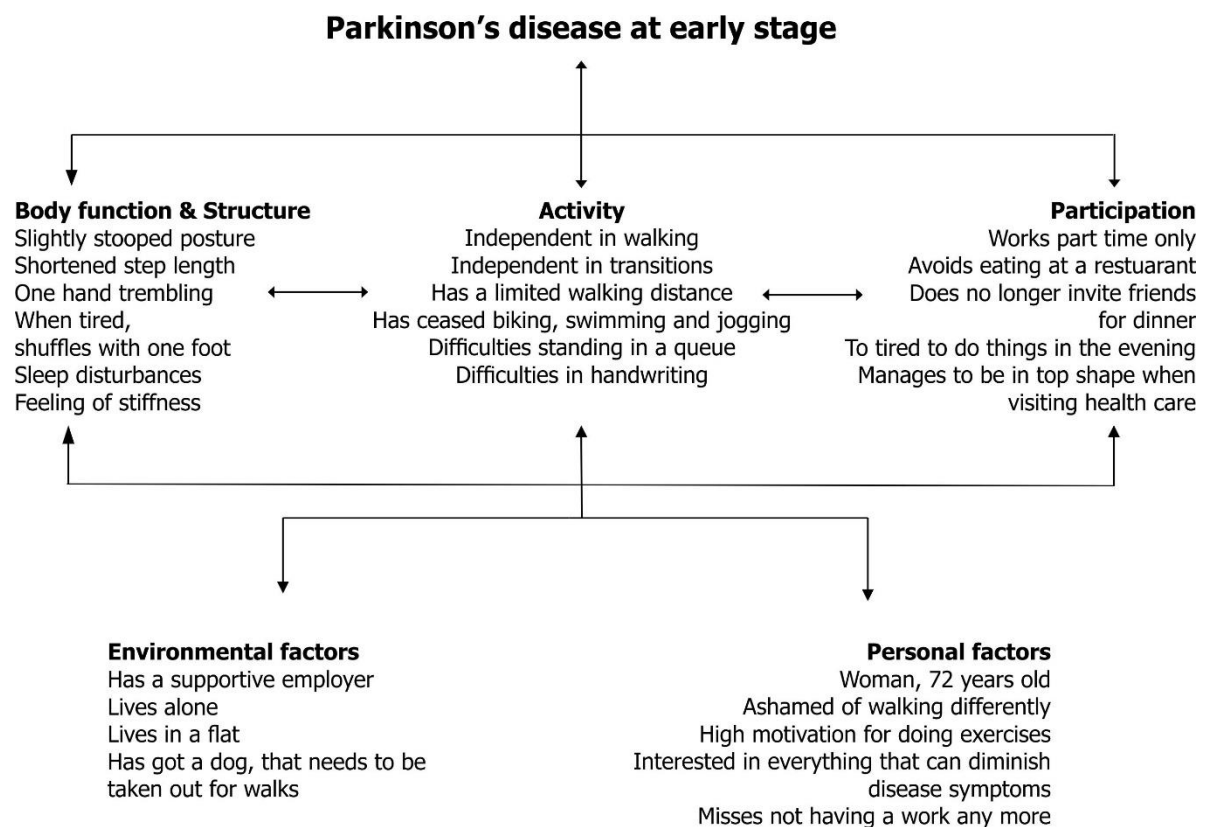


Figure 6. A fictive, yet representative person included in the thesis according to the ICF model.

3.3 SETTINGS

The studies included were carried out in the settings offered by the Swedish health care, the academic research environment, participants' homes, and in an exercise hall at the city centre. All clinical and laboratory assessments were made at Karolinska Institutet, in a research laboratory. The group training was carried out at 'Friskis & Sveltis', close to Stockholm city centre. Finally, the interviews were conducted at the participant's choice of place, most often in their homes but in a few cases in an undisturbed room at Karolinska University Hospital.

3.4 BALANCE TRAINING INTERVENTION

The 'Somatosensory Focused Balance Training without Cues' protocol was developed in discussion with long time experienced physiotherapists working with people having neurological diagnoses. Achieving exercises for enhancing focus on somatosensory input, and at the same time challenging each person's balance ability was the goal of the intervention. Moreover, from personal experiences of the physiotherapists, the context of training in group was considered both favourable for the ambiance when training and cost effective for the health care. A more detailed description of the exercises can be found in the thesis appendix.

The 'Somatosensory Focused Balance Training without Cues' was carried out during eight weeks, two sessions of 45 minutes/week. In addition to group training, participants were instructed to practice at home, daily; one to two exercises of their own choice, which they had found difficult to perform in the group session.

3.5 MEASUREMENTS

All measures used in the thesis are displayed in Table 2, marked according to the corresponding study and component within the ICF classification.

3.5.1 Body Function

Balance – According to the ICF classification, balance corresponds to the component 'body function'. However, this can be disputed, since dynamic balance is often judged when performing an activity such as walking, or in the Alternate Step Test used in this thesis. Accordingly, in this broadened interpretation of balance, tests used for balance or including balancing tasks were:

Studies I-II: the BBS ⁶², the BDL Balance Scale ⁶³, 10 m walk test⁶⁴, mUPDRS ⁶⁵, the TuG ⁶⁶.

Study III: the Alternate Step Test ⁶⁷ (Figure 7), an item included in the BBS. The task was used for evaluating the anterior/posterior CoP trajectory ⁶⁸ and the timing of movement phases. We selected this clinical task which had been difficult to perform, as noted in the non-published previous feasibility study. Also, deficits in the timing of sequential movements have been shown in PD ⁶⁹, and hence, this task seemed interesting to explore.

Study IV: the interviews provided information about the participants' perceived effect of the balance exercise intervention.

Cognition – Impaired cognitive ability was an exclusion criterion for participating in all studies, and the Mini Mental State Exam (MMSE) ⁷⁰ was used for screening. Normally the cut-off for cognitive impairment of the MMSE is 24 points ⁷¹. In the thesis, we used a lower cut-off of 22 points ⁷². Since one item has to do with drawing, and another item is answering a question of which floor level the respondent is at the moment, these questions were considered misleading. Taking into account the possible tremor in PD hand writing, and that the participants had been escorted to the third floor level from the entrance hall without information on where to go, we found a lower cut-off reasonable. Also, the reason to screen for exclusion was to ensure the ability to participate in the intervention – not the cognition per se. The TuG-cog ⁷³ was used for validation of the BDL Balance Scale, as dual tasking can reveal balance difficulties ⁷⁴.

Disease severity – The H&Y scale (below three for early PD) ¹⁰, was used as an inclusion criterion for participation. The more informative mUPDRS ⁶⁵ was used in the Studies I-III.

Posture – Shoulder-hip angle in relation to vertical, used in the supplementary thesis analysis.

3.5.2 Activity

Gait – The 10 m walk test ⁶⁴ is the most obvious walking test used in the thesis. Still, scores of the following tests, are also influenced by the walking ability; mUPDRS ⁶⁵, the BBS ⁶², the BDL Balance Scale ⁶³, the TuG ⁶⁶, and the TuG-cog ⁷³.

Activities in Daily Life –The participants had been instructed to start keeping an activity diary already before the first assessment. They noted all physical activities they considered as training, such as going for walks, horseback riding, dancing, and so on. The diaries were reviewed in conjunction with the assessments in Study II in order to evaluate possible changes in their weekly time spent on physical activities due to the intervention.

The participants narratives made in the interviews (Study IV) gave information on perceived improvements after training, such as the ability to stand on one leg, putting on trousers, feeling steadier when walking, and being able to walk faster, etc. The questions about activities in daily life were semi-structured, and their perceptions were expressed spontaneously in the course of interviews.

3.5.3 Participation

After termination of the last assessments, information of the participants' attendance or absence to the training was given by the training instructor. By the interviews in Study IV, we learned of their thoughts about having participated in the group training and about socializing in the group.

3.5.4 Environmental factors

Through interviews we got informed about how the early PD participants experienced traveling to the training, and other influencing factors. In connection to the first assessment they filled in forms about their civil state.

3.5.5 Personal factors

The neurologist provided data on their patients H&Y stage and the number of years since diagnose. In connection with the laboratory assessments we measured the participants' foot size. Interviews gave us knowledge about each early PD participant's mood and attitude towards participation in the study and towards life.

Table 2. The table displays the measures used in the thesis classified according to the corresponding component within the ICF model. The respective study, where applied, is marked with an x.

ICF component					Outcome measure	Study				
BF	A	P	EF	PF		I	II	III	IV	Thesis
	x				10 m walk	x	x			
				x	Age	x	x	x		x
	x				Alternate Step Test			x		
x	x				BDL Balance Scale	x	x			
x	x				Berg Balance Scale	x	x			
					Centre of Pressure trajectory			x		x
				x	Footsize					x
x					Shoulder-hip angle					x
x				x	Hoehn & Yahr scale	x	x	x	x	x
	x	x	x	x	Interviews				x	
x					Mini Mental State Exam	x	x	x	x	x
x	x			x	mUPDRS	x	x			
					Participation in intervention		x	x		
				x	Perceptions of training				x	
				x	Sex	x	x	x	x	x
	x				Timed Up and Go	x	x			
					Timed Up and Go-cognition	x				
	x	x			Timing of movement phases			x		
				x	Years since diagnose	x				

Abbreviations: BF=body function, A=activity, P=participation, EF=environmental factors, PF=personal factors mUPDRS=the motor part of the Unified Parkinson's Disease Rating Scale.

3.6 DATA COLLECTION

The clinical and laboratory tests of the early PD and the healthy controls were performed at the same occasion for each participant and by the same experienced assessor, a physiotherapist specialised in neurology. Moreover, for the early PD group, the timing for each occasion was carefully scheduled at the same time of day. The reason for this was to eliminate their performance from being biased by any fluctuation due to the time since medicine intake. Any changes in parkinsonian medication resulted in exclusion from the study.

The self-reported training diary noted by each early PD participant was kept starting from the eligibility assessment until termination of intervention, with the purpose to survey if the weekly time spent on training changed due to the intervention.

Study III, analysing the Alternate Step test demonstrated in Figure 7, used an equipment of 8 optoelectronic cameras (Elite 2002, BTS Milano) and two force plates (Kistler, Winterthur) for movement analysis, see Figure 7.

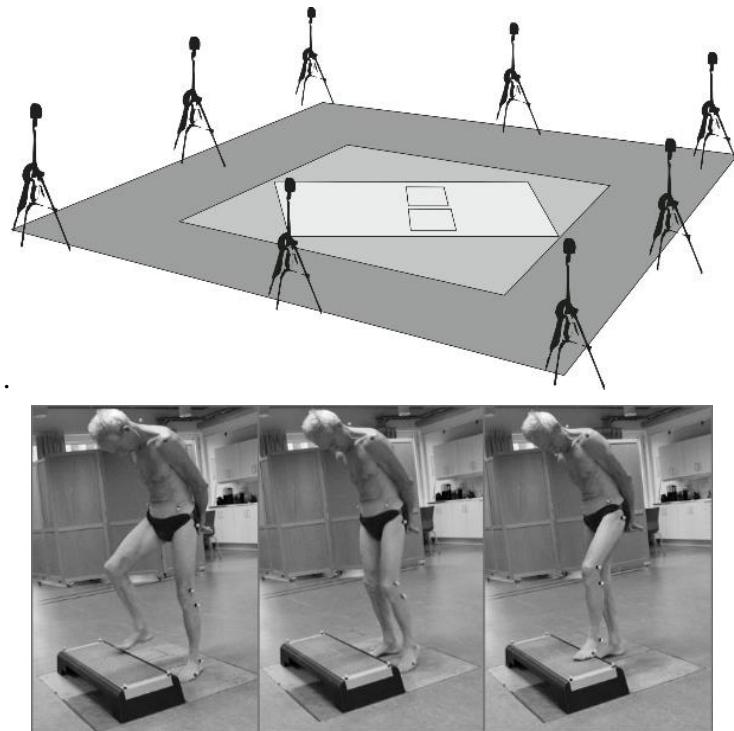


Figure 7. Illustration of the laboratory data collection of the Alternate Step Test. Above the research laboratory with two force plates in the middle, and eight optoelectronic cameras placed around the presumed target. Below, a person performing the Alternate Step Test task. Published with permission from the person on the photo.

Study IV, used semi-structured interviews to encourage participants to share their individual perspectives on their participation in the group exercise programme. The purpose of using a content analysis method was to explore perceptions not afforded by clinical outcome measures, searching to find new information ⁷⁵. Data was collected through face-to-face interviews, using a semi-structured interview guide allowing for deviations, if the interviewee or interviewer found that additional information was needed. The interview guide was derived from the study objectives, and consisted of key issues focusing on the experience of the community-based group balance exercise programme, what factors had influenced their participation, and of course their perceived effect on balance. The interviews were conducted by an experienced health professional and researcher, unaware of the participants' adherence to the training intervention. In order to facilitate for the respondents to speak freely, the interviewer had no previous connection to the study.

3.7 DATA ANALYSIS

3.7.1 Study I-III

All data was treated as non-parametric data, considering both the distribution of the data and the sample size^{76, 77}. Non-parametric effect sizes were calculated with ranked-biserial correlation from -1 to 1, where 0 is no effect⁷⁸. In this thesis, we interpreted the effect sizes as being large when reaching ± 0.6 , since it reflects that the outcome changed in more than 80% of the group. Statistical significance level was set to $p < 0.05$.

To validate the BDL in Study I, Spearman's rho, Cronbach's alpha, and Rasch analysis were used. In Study II - III we used medians and interquartile ranges for descriptive information. Significance tests were made by Mann Whitney U test and related samples Wilcoxon's signed rank test. An important aspect of the training evaluation in the Studies II - III was, at this point, to include only those who had participated in at least 50 percent of the training sessions.

3.7.1.1 Data processing and preparation in Study III

Laboratory movement analysis in Study III of the Alternate Step test was made of the sequential timing of the movement (divided into the four movement phases; approach, tread, return and double stance) and the CoP anterior/posterior trajectory. Data processing was carried out with the software Wolfram Mathematica 10.4. The laboratory data yields an enormous amount of information that needs to be systematically and carefully dealt with. By building a database within the program, and algorithms for mathematical definitions and calculations, we made the process of analysis as objective as possible.

To reinsure the reliability, graphs from the computerised analysis were visually inspected. In case of any ambiguous result, the video recording was overviewed. If faults in the data collection were found, the corresponding step cycles were excluded.

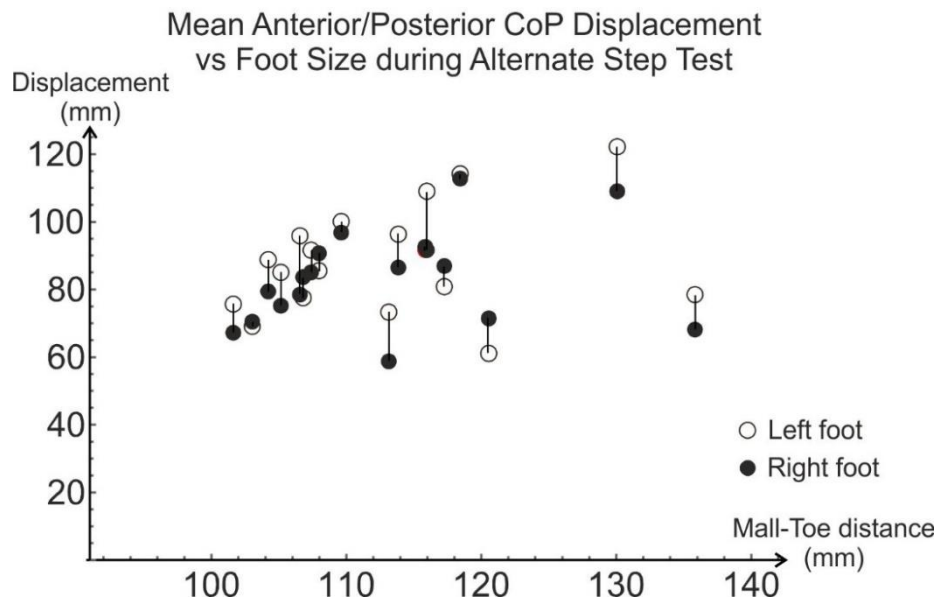


Figure 8. The diagram illustrates the correlation between foot size (Spearman's $\rho=0.32$) and Centre of Pressure (CoP) displacement in the Alternate Step Test, from a sample of healthy people within the thesis ($n=18$).

When calculating the CoP trajectory in Study III, a question was raised, if the foot size might have any importance. The analysis in Figure 8, shows the low correlation between CoP trajectory and foot size amongst our participants, Spearman's $\rho=0.32$. Therefore, we did not pay any respect to foot size in our further CoP analysis.

3.7.2 Study IV

The chosen qualitative design chosen of content analysis looked for knowledge and understanding by manifest and latent interpretation of the content in the transcribed interviews through the systematic process of coding and identifying themes⁷⁹. The researcher conducting the interviews was included as one of the researchers doing the analysis, together with the assessor of the other studies. Accordingly, the transcribed interviews were analysed by the two researchers, each one separately, defining meaning units and condensed meaning units. Thereafter, they met to discuss and agree on their meaning units. Discussions on the interpretation of underlying meanings were made, and triangulated for accordance on categories with a third experienced researcher, before finally consensus was reached between the three researchers on sub-themes, themes and overall theme.

3.7.3 Supplementary Thesis Analysis

Because of the ongoing scientific discussion about whether the impaired somatosensory integration can have an effect on posture^{26, 30, 31}, we decided to perform an additional analysis where we looked at the posture in early PD in comparison to healthy, and in early PD before and after the Somatosensory Focused Balance training without Cues.

To define the best method to evaluate posture, we compared different ways of calculation from the same trials of the healthy controls assessment when standing still for 60 seconds, see Figure 9. It was very clear that the measure using the shoulder-hip angle in relation to the vertical plane gave the smallest variation within the group, and was the most consistent measure.

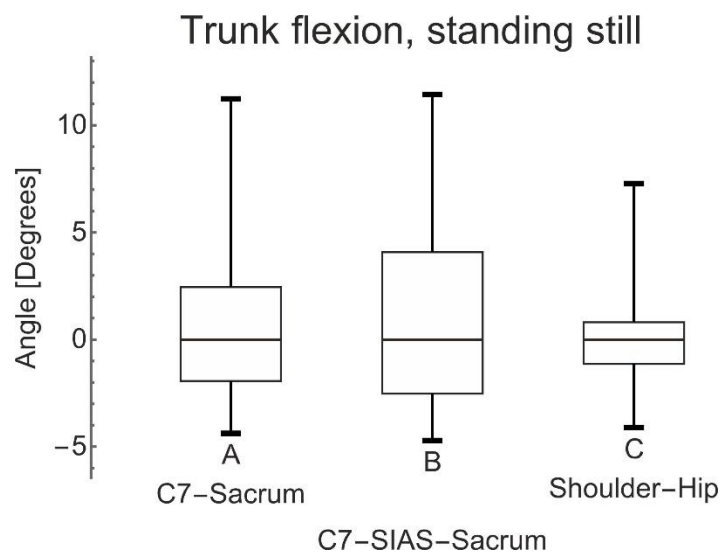


Figure 9. Illustration of how result differs from the same trials, depending on choice of reference markers. The boxplots show medians, interquartile range and full range from a sample of the healthy participants in the thesis (n=15).

Before training intervention, using the shoulder-hip angle calculation, we performed a comparison of posture between the healthy control group and the early PD group. There was a significant difference, showing a more flexed posture in the early PD group, $p=0.03$, Mann-Whitney U test, see Figure 10.

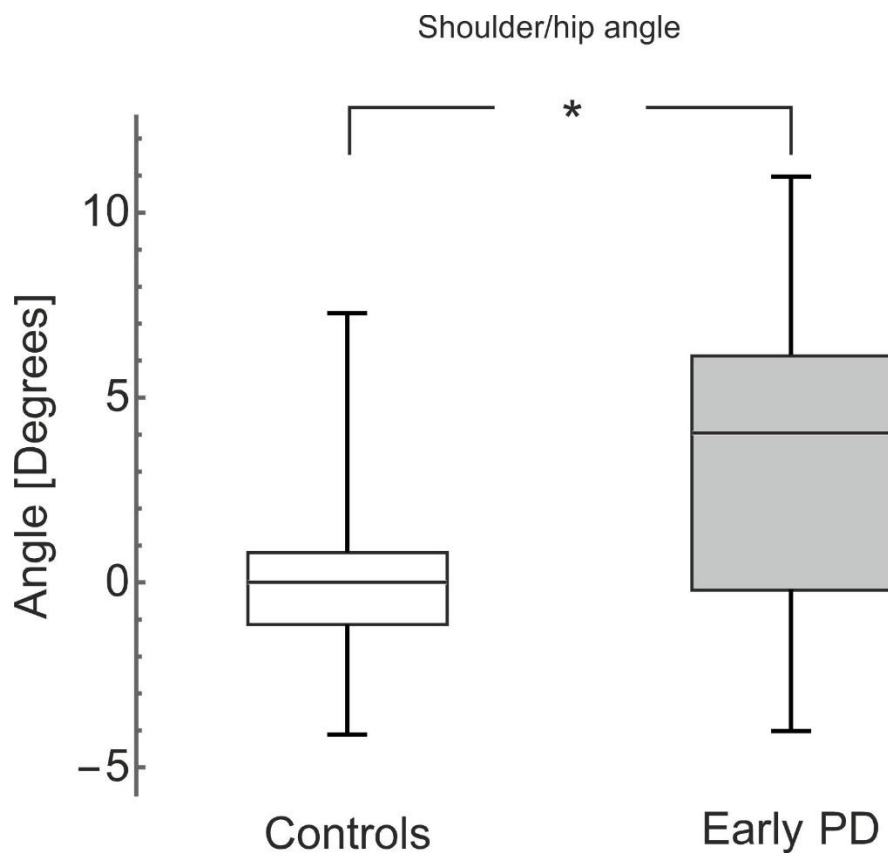


Figure 10. The boxplots show mean, interquartile ranges (IQR) and min/max trunk flexion measured from hip and shoulder markers when standing still during 60 sec, controls (n=15) and early PD (n=25), $p=0.03$ Mann-Whitney U test.

3.8 ETHICAL CONSIDERATIONS

Ethical approval for all studies were obtained from the local ethics committee of the Karolinska Institutet in Stockholm, Sweden diary no 2005/179-31, 2008/276-32, 2010/414-32, 2016/472-32. All participants gave their written consent to participate, after verbal and written information. They were informed that they could withdraw at any time without any explanation, or any influence on their continued care. The participants were also asked for written consent to being photographed for use in the studies, thesis and education, and most of them gave their permission.

During the course of the thesis, the study plan expanded from including laboratory measures only, to embrace clinical measures as well. This initiative was made by me, as a PhD student, not being aware of that a supplementary ethic application requesting approval of the added clinical measures were needed. It happened during the time of change of main supervisor, as the first main supervisor went into retirement. I, alone, am responsible for this mistake. However, approval for the added measures was obtained by the local ethics committee in retrospect, diary no 2016/472-32.

4 RESULTS

4.1 MEASURING BALANCE IN EARLY PARKINSON'S DISEASE

4.1.1 Clinical assessment

In Study I⁸⁰, the BDL balance scale was shown to reach neither ceiling nor floor effects in our population of early PD. The correlation to the common Berg Balance Scale was good, despite the fact that the Berg Balance Scale did reach ceiling when performed by this population. The Rasch analysis showed a good distribution of the individual items difficulties, although one item, walking in stairs, did not fit the model. The Cronbach's alpha test reliability was 0.83, a very good result considering the sample size.

In addition, the BDL balance scale was able to reveal a balance deficit between early PD and healthy, whereas the BBS could not, see Figure 11. We therefore concluded the BDL balance scale to be appropriate as main outcome in our subsequent training study, evaluating the effect of the 'Somatosensory Focused Balance training without Cues'.

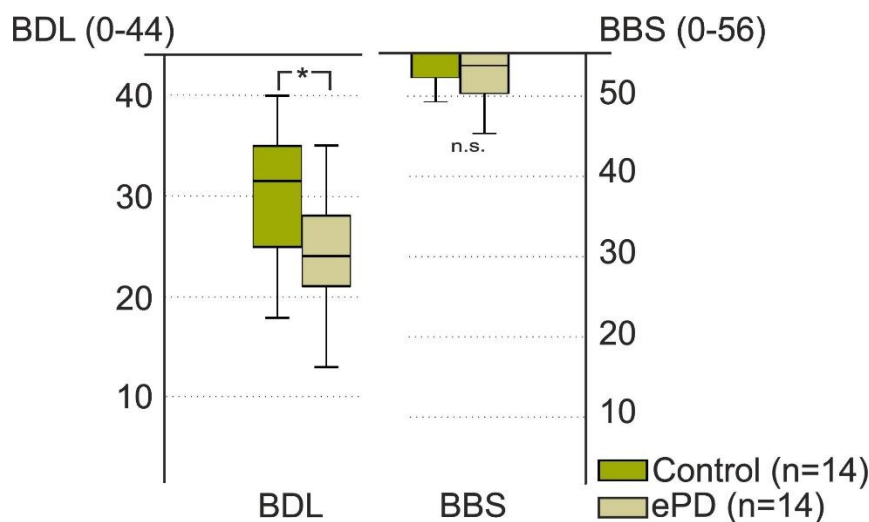


Figure 11. Boxplots of early PD and healthy age- and sex-matched people performing the BDL Balance Scale and the Berg Balance Scale.

* $p < 0.05$, Independent samples Mann-Whitney U test.

Abbreviations: BDL=BDL Balance Scale, BBS=Berg Balance Scale, n.s.=non-significant.

4.1.2 Laboratory assessment

In Study III, a method of laboratory based movement analysis of dynamic balance with the Alternate Step Test was developed. Using this method, movement analysis showed that people with early PD were both slower and applied a shorter anterior/posterior displacement of the CoP when performing this dynamic balance task (the Alternate Step Test) compared to healthy age- and sex-matched, see Table 3.

Table 3. Comparisons between early PD and Healthy Controls, and between early PD before and after Somatosensory Balance training without Cues.

	ePD vs Healthy Controls <i>p-value</i> ¹	Effect Size ²	ePD before training vs after training <i>p-value</i> ³	Effect Size ²	ePD after training vs Healthy Controls <i>p-value</i> ¹	Effect Size ²
Total cycle time	0.018*	0.42	0.001*	-0.96	0.882	-0,03
Relative phases:						
Approach	0.032*	-0.39	0.031*	0.60	0.974	0.01
Tread	0.608	0.09	0.055	-0.53	0.077	-0.35
Return	0.242	-0.19	0.193	0.36	0.668	0.09
Double stance	0.037*	0.47	0.687	-0.11	0.067	0.36
CoP	0.002*	-0.51	0.009*	0.60	0.276	-0.22

¹Independent-samples Mann-Whitney U test, ²Rank biserial correlation, ³Related-samples Wilcoxon signed rank test. ePD= early Parkinson's Disease. * indicates a significant change $p < 0.05$

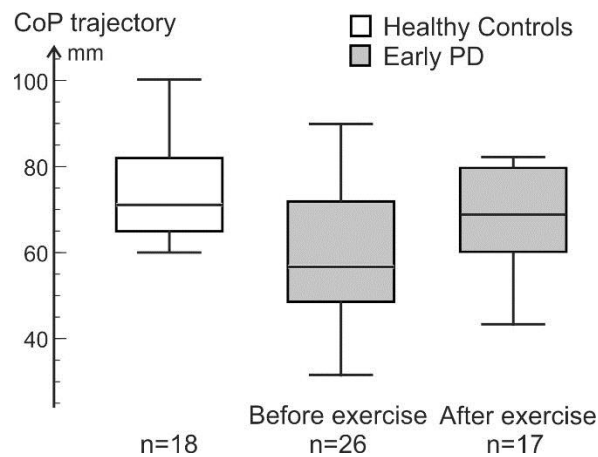


Figure 12. The Centre of Pressure (CoP) anterior/posterior mean maximum displacement when performing an Alternate Step Test cycle. Boxplots showing median, interquartile ranges and min/max of healthy age- and sex- matched people, and of early PD before and after balance exercise intervention.

4.2 EFFECT OF THE ‘SOMATOSENSORY FOCUSED BALANCE TRAINING WITHOUT CUES’

The effects from the targeted exercise intervention, evaluated in Study II-IV, are presented according to the ICF classification. In Table 4, changes in the corresponding body function and activity components are summed, and in heading 4.2.2 aspects on environmental and personal components are further presented.

4.2.1 Effect on Body Function and Activities

Table 4 puts together the results from the different quantitative measures in the Study II and III in relation to the corresponding component in the ICF classification.

After the balance exercise intervention, differences seen between the early PD group and healthy control group in Study III, were no longer significant, see Table 3 and Figure 12.

Table 4. Results from the outcomes measures in Studies II -III and the supplementary thesis analysis.

Outcome measure	p-value ¹	Effect size
10 m walk speed	0.012*	0.61
Alternate Step Test	0.001*	-0.96 ³
Anterior/posterior CoP	0.009*	0.6
BBS	0.007*	0.3
BDL Balance Scale	0.005*	0.53
Shoulder-hip angle	0.041* ²	0.52
mUPDRS	0.027*	-0.47
Timing of movement phases	No difference after training compared to controls	
TuG	0.948	0.02

¹ * indicates a significant change $p < 0.05$, related samples Wilcoxon signed rank test

² The significance is towards a more stooped position!

³ The effect size of mean step time is negative, in this case implying higher velocity

The qualitative interviews in Study IV gave us important complementary information; the large number of comments on perceived improved stability when dressing, and a feeling of being steadier when walking, as well as being able to walk faster, reinforced the result of the quantitative measures.

4.2.1.1 Posture

After the training period, we found a significant change towards an increased shoulder-hip angle (more stooped posture!) when standing still compared to before the training, see boxplots in Figure 13. The training did not improve the posture.

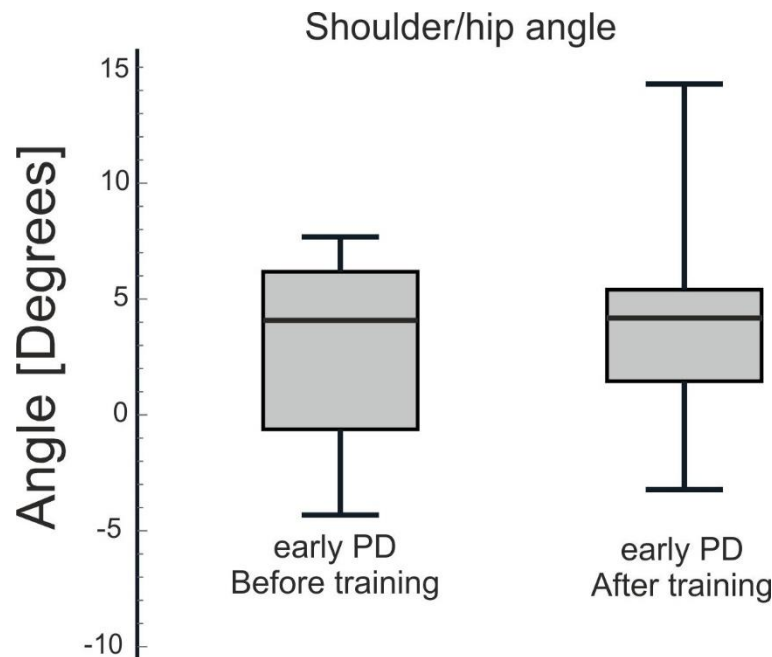


Figure 13. The boxplots show median, interquartile range and total range of shoulder-hip angle in early PD ($n=17$) measured from hip and shoulder markers when standing still during 60 sec, before and after 'Somatosensory Focused Balance training without Cues', $p=0.041$ related samples Wilcoxon signed rank test.

4.2.2 Personal and Environmental aspects

From the interviews we learnt that the context of the intervention, training with peers in central Stockholm on fixed days and with an experienced instructor was perceived to be of utmost importance to maintain training. Many participants had wished the training to continue as an ongoing activity, because they found training important. Furthermore, the group balance training provided peer support as well as exercise, which was valued by the participants. Both aspects empowered them to cope with their disease. The group context met many of the diverse needs in early Parkinson apart from the exercise effect. Importantly, participants' comments highlighted their joy and satisfaction with taking part in a group, together with their need for exercise on a regular basis under supervision of a leader. They confessed that exercising does not happen on one's own. The overall theme from the Study IV, was consented to 'The group is the glue', final themes and categories are presented in Table 5. The group camaraderie seemed to have been the major factor for the compliance to the training.

Table 5. The table presents categories, themes and overall theme derived from the qualitative content analysis study, Study IV.

OVERALL THEME	THEMES	CATEGORIES
The group is the glue	My body is my limit	Every day a struggle
		In the mind of others
		I never get well
	Exercise – a bare necessity	To keep up the good work
		With a little help from my friends

4.2.2.1 Environmental aspects influencing participation

A few drop-outs from training were due to heavy snowfall and badly cleared roads during winter, making it difficult to travel. Another drop-out was caused by the early morning start time of the group training, combined with a long travelling distance, see the flow chart in Figure 5.

4.2.3 Long term effects

From the follow-up assessment in Study II, (n=9)⁸¹, we could establish that the improvements achieved made by this group after training, had declined after 6 months, and that the result from the clinical assessments were almost back on the same level as prior to the training intervention.

5 DISCUSSION

This thesis has made a thorough evaluation of the hypothesis based balance training intervention of ‘Somatosensory Focused Balance training without Cues’ for people with early PD. To our knowledge, this is so far the only time this balance training approach is evaluated, and consequently the first time for people with early PD.

Furthermore and to our knowledge, is it the first time the Alternate Step Test, an item of the Berg Balance Scale, was explored in a movement laboratory. Considering the purpose of evaluating a hypothesis based training approach, we found that clinical outcome measures were not sufficient. Therefore, we chose to look deeper into the movement quality by laboratory movement analysis. Again, there was no obvious tool for measuring the dynamic balance within a movement laboratory, and, consequently, we created a model for this purpose by use of the Alternate Step Test. To further deepen our understanding of the participants' own perception of the training, the qualitative interview study was a valuable contribution.

5.1 MAJOR FINDINGS

The BDL Balance Scale proved to be a valid outcome measure for use in balance assessment in early PD. Moreover, the training approach of ‘Somatosensory Focused Balance training without Cues’ had a positive effect on body functions and activity limitations in our population. We saw a significant improvement in most of the chosen clinical outcomes, and the improvements were confirmed by laboratory outcomes as well as by the participants themselves when interviewed. In addition, the aspect of training in a group with peers influenced the participants’ mood and motivation in a positive way, and the group context contributed to their adherence to the training.

According to the ICF, most of our chosen outcomes are classified as components of body function and activity. This was considered appropriate, as the balancing ability, has been found to be the major factor influencing gait and mobility in PD ⁸².

5.1.1 Measuring balance in early Parkinson’s Disease

In the clinics, there is a rich palette of balance tests used by physiotherapists. After the work with this thesis started, a few new scales intended for measuring balance in PD have emerged, the BESTest and the shortened Mini-BESTest, showing both strengths and limitations when used for the early PD population ^{83, 84}.

Based on our current knowledge and experiences, the BDL balance scale can be considered a suitable choice to evaluate balance in early PD. Firstly, the BDL balance scale comprises items described as balance challenges in everyday life by people with PD, unlike other composite balance tests. Secondly, the BDL was shown to distinguish people with early PD in our project from healthy age- and sex-matched controls. Thirdly, the BDL balance scale does not have either ceiling or floor effects in the early PD population. Finally, the test is

fairly quick to perform and does not need any special equipment, making it easy to administer and feasible to carry out in the clinics. However, the BDL balance scale lacks an item with walking turns. Such an item needs to be added to the scale, since turning has been shown to be a sensitive indicator of postural instability in PD ⁸⁵⁻⁸⁷. For that reason, when using BDL for assessing balance in early PD, a complementary test including walking turns needs to be performed.

Nevertheless, despite the many existing balance tests used by physiotherapists, and taking into account the suggested improvements of the BDL balance scale in the thesis study I, Claesson et al.⁸⁰, an adequate and comprehensive test for use with PD, especially for early PD, targeting the very specific balance difficulties arising along with the disease progression, is still needed.

5.1.2 Balance in early Parkinson's Disease compared to healthy

In our studies, differences in balance performance were confirmed between early PD and healthy age- and sex-matched controls by their performance of the BDL balance scale and by performance of the Alternate Step Test. This is in line with earlier studies that also show that balance is affected already at an early stage ^{88, 89}.

5.1.3 Balance in early Parkinson's Disease before and after intervention

The outcomes indicate that people with early PD improved their balance after the intervention ⁸¹. Not only the clinical balance assessment, but also the laboratory assessment and the interviews pointed towards a positive effect on balance performance. From the assessments, and reinforced by the interviews; we concluded that every day activities like, for example, standing on one leg putting on trousers had become easier, and that walking had become safer and faster. These are tasks often reported as problematic by people with PD ^{8, 90}.

Compared to many other training intervention studies, often with sessions three times a week during 10-12 weeks ^{52, 60, 91}, the 'Somatosensory Focused Balance Training without Cues', was carried out twice a week for eight weeks. This was considered closer to what is achievable in the usual health care settings in Sweden. Even with the moderate inclusion criterion of having participated at least half the sessions, we could still detect an improvement in balance performance. In addition, by means of their training diaries, we were confident that the improvements made were not due to a sudden increase in their usual amount of training outside the intervention.

That balance training is important for gait and mobility in PD was highlighted by Christoforetti et al ⁸². They found a strong predictive relationship between balance, gait and mobility limitations, regardless age, disease severity, fall history, or other demographic aspects. Moreover, they concluded that balance was the major factor influencing these limitations, and suggest, in line with our intervention, that targeted balance training may be particularly important for the improvement of mobility and gait in people with PD.

5.1.3.1 Long-term aspects

At six months follow-up, improvements made after the intervention had vanished, and participants showed again the same result as before the intervention. This means that much of the gain from training had been lost. On the other hand, due to the progressive character of the disease, some deterioration should be expected. Many respondents in Study IV acknowledged their difficulties in taking the responsibility for training by themselves, and wished for an opportunity of continued guided training.

A recently published review evaluating exercise in PD ⁹², concludes evidence of a minimum duration for eight weeks of balance training to have persisting effects after 3–12 months. Unfortunately, their study lacks information on recommended intensity and frequency of training. According to their findings, our training intervention may not have lasted long enough, or have been sufficiently intense, for long-term effects to be expected.

5.1.3.2 Possible underlying mechanisms

Previous research declares the basal ganglia as being critical for central processing of postural control, and in particular for the integration of sensory information ⁴. Today, evidence of exercise-induced neuroplasticity in PD is growing ⁴⁹. Interestingly a recent study showed neuroplasticity changes in the dopaminergic signalling after exercise in people with early PD ⁹³. Seeing that balance performance has improved after the targeted intervention of ‘Somatosensory Focused Balance training without Cues’, a quick conclusion could be that this targeted training intervention did enhance the processing of sensory information within the basal ganglia.

On second thought, after ending this project, we cannot jump to any certain conclusion of the underlying mechanism for the participants’ improvements in balance performance. There are indeed several mechanisms apart from neuroplasticity that may have contributed to the improvement, such as reduced muscle rigidity or bradykinesia, increased self-confidence in movement, or the aspect of motor learning strategies for balance. To obtain a deeper understanding of the possible effects within the brain, a complementary evaluation with fMRI and Brain-Derived Neurotrophic Factor (BDNF) before and after the exercise intervention would have been elucidative. Nota bene, a possible change in these outcomes cannot give any specific information on the change of somatosensory integration for balance.

5.2 METHODOLOGICAL CONSIDERATIONS

There are several methodological concerns to address before finalizing the thesis results. The original plan of the thesis was designed as a cross-over study, with power based on calculations from the laboratory outcome measures. Mainly due to unforeseen environmental factors, several participants dropped out from one of the randomised training groups forcing us to merge the groups to get enough statistical power. Considering the progressive course of PD, and the many disparate difficulties connected with the disease, larger groups, overshooting the estimated statistical power goal would have been more appropriate.

5.2.1 Choice of methods

In Study I, validating the BDL scale for early PD, a standard scale specific for balance in this population was warranted. Since such a standard did not exist, the second best alternative was to correlate the BDL to similar scales, to disease severity scales, and to the most often used balance scales in this population. Later, new recommended scales assessing balance in PD have come up, in particular the BESTest^{94, 95}. The shortened form, the mini-BESTest, was subsequently translated to Swedish⁹⁶, and would have been added to both the validating and training evaluation studies if it had existed earlier.

A laboratory based movement analysis for measuring dynamic balance did not exist. Therefore we developed a new method using the Alternate Step test for this purpose. The method showed to be an accurate and feasible outcome measure for the thesis population.

5.2.2 External validity

An important limitation is the number of participants and the convenience sample. Nevertheless, the many different approaches; clinical, laboratory movement analysis and interviews, for evaluating the intervention of ‘Somatosensory Focused Balance Training without Cues’ strengthen the trustworthiness of the result. Therefore, the improvements made provide incentive for future research.

5.2.2.1 Generalisability

Our results are based on participants at an early stage of PD and their comparisons to healthy age- and sex-matched controls. The people that dropped out from the training intervention, did not differ from the other participants regarding disease severity, age or sex. All participants had volunteered, and thus curiosity and interest in research may be attributed to the subjects. Moreover, the early PD participants volunteered to take part in a training intervention. Therefore, people with PD not interested in training would probably not have reported themselves for participation. Consequently, this affects the generalisability of the result.

Even so, we do believe that other people with early PD taking part in a similar intervention, would undergo the same positive impact as those included in our study. Naturally, the intervention appeals mainly to those who are comfortable with training in a group, and the adherence was highly connected to the satisfaction of sharing experiences in a group. The effect of the training, if applied in a single person-to-therapist situation, is not possible to deduce.

5.2.2.2 Context

The context of the included studies; being part of ongoing research, the exercise location, and the experienced group training instructor may have played an important role for the result.

The assessments were carried out at Karolinska Institutet research laboratory, this might have contributed to a perception of earnestness and correctness, making the participants feel

important and perform at their best. This also guaranteed for the assessments being conducted in the same way and under the same circumstances each time.

The training intervention was carried out close to the city centre at an exercise location where healthy community dwelling people exercise. The fact that the training location was not part of the health care facilities, might have contributed to a feeling of being less stigmatised by the disease and a part of the municipal everyday life. We learnt that travelling distance and transport facilities are important for being able to participate, and needs to be taken into account when planning for interventions. In order to form groups, the context of a larger community with proper municipal means of transport is necessary.

An experienced physiotherapist was recruited to supervise the targeted training. To customise the exercises individually for each participant and to remain loyal to the concept of 'Somatosensory Focused Balance Training without Cues', knowledge of balance training and expertise in providing personal feedback was vital.

5.2.3 Internal validity

The hypothesis of 'Somatosensory Focused Balance Training without Cues', was tested in this thesis. The intervention approach, targeting conscious focus on somatosensory input for maintaining balance, is hypothesis based. We cannot be sure that our specifically developed exercise programme really promotes an enhanced somatosensory integration. Even though improvements in balance performance were reached by our outcome measures and reinforced by the participants' narratives, it is not sufficient as evidence for the hypothesis. On the other hand, although the underlying mechanisms for the improvements made remains uncertain, the targeted intervention has clearly been beneficial for improving the participants' balance performance.

5.2.3.1 Sampling validity and transferability in Study IV

One can question how accurate the interviewed sample in the Study IV represents the population of early PD. Ideally, in content analysis research, the sampling should be actively and strategically planned for ensuring representativeness. In this case, and of pragmatic reasons, all participants in the delayed start training group (n=15) were asked to participate and they all agreed. People with early PD, not interested in training, nor in participating in a research study, cannot be considered represented in this study sample. Moreover, in order to get insight in possible transfer of our result to other cultural settings, further investigation is needed.

5.3 CLINICAL IMPLICATIONS

- The BDL balance scale can be recommended as a clinical outcome measure for balance evaluation in early PD.
- The ‘Somatosensory Focused Balance Training without Cues’, can contribute to balance improvement in early PD. This was shown by clinical outcomes, by laboratory movement outcomes, and reinforced by participants’ perceptions.
- The context of training should be considered as highly important. Our study population found it difficult to maintain continuous training on their own, and the regular supervised training in a friendly atmosphere among peers overcame these difficulties. Moreover, training in a group seems to have contributed to a positive attitude towards training and a higher motivation for training. The possibility to meet peers, and to feel part of the society's community can give unexpected positive effects on the motivation for training and reduce the stigma of the disease.

5.4 FUTURE RESEARCH

A future goal, considering the expanding costs for our health care system, will be to select the most cost effective intervention. Therefore, future research where different balance exercise interventions for people with PD are compared and explored according to design, length, intensity, context and to disease severity is requested

The number of scientific studies about the positive effect of exercise in PD are growing, as well as evidence of that exercise can trigger neuroplasticity changes in the human PD brain. Regarding the positive effects from the ‘Somatosensory Balance Training without Cues’, more research on this targeted intervention with fMRI or BDNF outcomes is proposed in order to further explore the original hypothesis.

The Alternate Step Test is an appropriate test of dynamic balance, for use in research laboratory movement analysis.

There is still a need for a targeted balance scale used for evaluating balance performance in PD throughout the progression of the disease. This could be a development of the BDL balance scale. One such important aspect to include, would be to add an item assessing the ability to turn around while walking.

5.5 CONCLUSIONS

‘Somatosensory Focused Balance Training without Cues’, can improve balance in early PD. The improvement was reflected within clinical balance outcomes and by laboratory movement analysis. From the interviews in Study IV, participants’ narratives confirmed important improvement in balance after group training, and that they highly appreciated making friends with peers who contributed to a higher motivation for training.

In addition, the results from the thesis show that the BDL is a valid clinical assessment tool for use when measuring balance in early PD.

Furthermore, the Alternate Step Test showed to be a feasible test for evaluating dynamic balance within the movement analysis laboratory setting.



EPILOGUE

*"Well, Ingrid, I'm getting tired of you and your ongoing blablabla
about somsomry...eh, whatever.*

I couldn't care less.

You see, I have met some new friends now; we go for walks, and we play boules.

I'm getting by with a little help from my friends.

I'm too busy to spend more time on you and your ideas. Sorry, enough for me.

I'm off. So long."

I answered: "That sounds good, enjoy! Good bye!"

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8 APPENDIX

DESCRIPTION OF THE 'SOMATOSENSORY FOCUSED BALANCE TRAINING WITHOUT CUES'

AIM: To impose the use of cerebral somatosensory feedback (proprioception and touch) for maintaining balance.

FRAMEWORK FOR THE TRAINING PROGRAM INTENTION: The integration of somatosensory feedback with the visual and vestibular feedback in balancing has been shown to be impaired in Parkinson's disease:

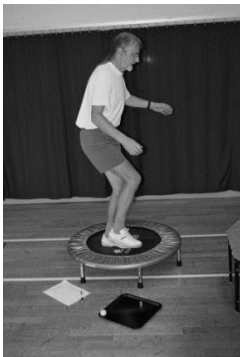
The idea was to perform challenging balance exercises with imposed focused attention on the somatosensory input for maintaining balance control. Participants were to perform balance exercises where vision was obstructed or distracted from contributing to balance control. Due to its complexity, vestibular input was not manipulated. In addition, all types of movement facilitators, for example external cues, were excluded.

TRAINING PROGRAM CONTENT: Exercises were individually adjusted to be sufficiently challenging for every participant. Difficulties within each exercise were raised successively by narrowing the stance of support, changing from hard to moving support surface, blindfolding the eyes or by turning the head/body. Many exercises were performed in pairs. The training was supervised by a skilled and experienced physiotherapist.

All photos are taken by Hjalmar Wåhlin.

The people on the photos have given their written consent.

EXAMPLES OF EXERCISES:



Walking or jogging on the spot on a trampoline puts a great demand on the attention on somatosensory input. The timing and force have to be continuously adjusted according to the elasticity of the trampoline. This was an exercise that most of the participants found difficult and challenging. For those who were really skilled, the task was made more difficult by making sudden stops, balancing on one foot, before continuing again.



Balancing on a trampoline (a moving surface that imposes focused attention to somatosensory input) and at the same time rolling a ping-pong ball along the sides on a tray (distracting vision from maintaining balance).



Walking heel to toe, keeping a ping-pong ball on a tray, while turning the upper body from side to side.



Moving back and forth and sideways in the room keeping a ball in between each other's chests, avoiding it from falling down. You need to focus on the somatosensory input to keep the right amount of pressure on the ball while moving. The challenge gets even higher if you close your eyes, or if you put the ball in between your backs instead.



Having a tug of war with a rope forces you to pay attention and respond to the pull you get from the other part by a hold or pull back. When you pull your partner towards you, an intricate somatosensory feedback from feet and body is used to create the force.



Attempting to push each other off balance with a ball in between the chests, trying not to fall and not to let the ball drop into the ground.



Standing on a trampoline on one leg, drawing circles in the air with the other leg. Those who dared, tried it with their eyes closed.



Standing on air-filled cushions making squats, even more difficult with eyes closed. For those who found that too difficult, the same task was performed on foam squares.